PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

| Applicant's or agent's file reference BOR00006/WO | FOR FURTHER ACTION as | see Form PCT/ISA/220 well as, where applicable, item 5 below. |
|---|---|--|
| International application No. | International filing date (day/month/year) | (Earliest) Priority Date (day/month/year) |
| PCT/DK2004/000282 | 23/04/2004 | 23/04/2003 |
| Applicant BOREAN PHARMA A/S | | |
| according to Article 18. A copy is being t | , | Authority and is transmitted to the applicant |
| · · · · · · · · · · · · · · · · · · · | s of a total of <u>6</u> sheets. by a copy of each prior art document cited in t | his report. |
| Basis of the report With regard to the language, the language in which it was filed, un | e international search was carried out on the nless otherwise indicated under this item. | basis of the international application in the |
| this Authority (R | ule 23.1(b)). | enslation of the international application furnished to |
| | und unsearchable (See Box II). | |
| 3. Unity of invention is la | cking (see Box III). | |
| 4. With regard to the title, | | |
| <u></u> | submitted by the applicant. | the section Section 1999 |
| the text has been establ | ished by this Authority to read as follows: | |
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| | | |
| 5. With regard to the abstract, | | $\langle x_i x_i^2 \rangle = \frac{1}{2} \frac{1}{w_{ij}} \left(\frac{1}{2} \left(x_i x_{ij} x_{ij}$ |
| X the text is approved as s | submitted by the applicant. | |
| the text has been establ may, within one month f | ished, according to Rule 38.2(b), by this Autt rom the date of mailing of this international s | nority as it appears in Box No. IV. The applicant earch report, submit comments to this Authority. |
| 6. With regards to the drawings , | | |
| <u> </u> | published with the abstract is Figure No | · |
| as suggested by | | |
| as selected by t | his Authority, because the applicant failed to | suggest a figure. |
| as selected by t | his Authority, because this figure better chara | acterizes the invention. |
| b. X none of the figures is to | be published with the abstract. | |

Form PCT/ISA/210 (first sheet) (January 2004)

with the state of the first of the state of

International application No.

PCT/DK2004/000282

| Box | No. I | Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet) |
|-----|---------------|---|
| 1. | With inver | regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed ition, the international search was carried out on the basis of: |
| | a. | type of material X a sequence listing table(s) related to the sequence listing |
| | b. | format of material X in written format X in computer readable form |
| | c. | time of filing/furnishing X contained in the international application as filed X filed together with the international application in computer readable form furnished subsequently to this Authority for the purpose of search |
| 2. | | In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished. |
| 3. | Addit | ional comments: |
| | | |
| | | |

International application No. PCT/DK2004/000282

| Box II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet) |
|--|
| This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons: |
| 1. Claims Nos.: because they relate to subject matter not required to be searched by this Authority, namely: |
| Claims Nos.: because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically: |
| 3. Claims Nos.: because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a). |
| Box III Observations where unity of invention is lacking (Continuation of item 3 of first sheet) |
| This International Searching Authority found multiple inventions in this international application, as follows: |
| see additional sheet |
| |
| 1. As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims. |
| 2. As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee. |
| 3. As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.: |
| 4. No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: |
| Remark on Protest The additional search fees were accompanied by the applicant's protest. X No protest accompanied the payment of additional search fees. |

International Application No PCT/DK2004/000282

A. CLASSIFICATION OF SUBJECT MATTER IPC 7 C07K19/00 C12N9/64

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols) IPC 7 C12N C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, BIOSIS, EMBASE, Sequence Search, WPI Data, PAJ, CHEM ABS Data

| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. |
|------------|---|-----------------------|
| A | HARRIS J L ET AL: "Definition and redesign of the extended substrate specificity of granzyme B." THE JOURNAL OF BIOLOGICAL CHEMISTRY. 16 OCT 1998, vol. 273, no. 42, 16 October 1998 (1998-10-16), pages 27364-27373, XP002296677 ISSN: 0021-9258 cited in the application abstract -/ | 1-39 |

| X Further documents are listed in the continuation of box C. | χ Patent family members are listed in annex. |
|---|---|
| Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier document but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed | *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art. *&* document member of the same patent family |
| Date of the actual completion of the International search 12 November 2004 | Date of mailing of the international search report 0 2. 12. 04 |
| Name and mailing address of the ISA European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo ni, Fax: (+31-70) 340-3016 | Authorized officer Montrone, M |

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International Application No PCT/DK2004/000282

| C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT | | | | | | |
|--|---|-----------------------|--|--|--|--|
| Category ° | Citation of document, with indication, where appropriate, of the relevant passages | Relevant to claim No. | | | | |
| A | SUN JIURU ET AL: "Importance of the P4' residue in human granzyme B inhibitors and substrates revealed by scanning mutagenesis of the proteinase inhibitor 9 reactive center loop" JOURNAL OF BIOLOGICAL CHEMISTRY, vol. 276, no. 18, 4 May 2001 (2001-05-04), pages 15177-15184, XP002296678 ISSN: 0021-9258 cited in the application abstract | 1-39 | | | | |
| A | WO 03/010204 A (KIM JEONG-MIN; CHO TAE-HOON (KR); LEE WOO-JONG (KR); PARK HEUNG-BOK () 6 February 2003 (2003-02-06) cited in the application abstract page 3, lines 8-32 page 5, line 29 | 1-39 | | | | |
| A | US 6 010 883 A (THOEGERSEN HANS CHRISTIAN ET AL) 4 January 2000 (2000-01-04) cited in the application abstract column 2, lines 1-40 | 1-39 | | | | |
| A | SUN JIURU ET AL: "Expression and purification of recombinant human granzyme B from Pichia pastoris" BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, vol. 261, no. 2, 2 August 1999 (1999-08-02), pages 251-255, XP002296679 ISSN: 0006-291X abstract | 1-39 | | | | |
| A | ROTONDA J ET AL: "THE THREE-DIMENSIONAL STRUCTURE OF HUMAN GRANZYME B COMPARED TO CASPASE-3, KEY MEDIATORS OF CELL DEATH WITH CLEAVAGE SPECIFICITY FOR ASPARTIC ACID IN P1" MOLECULAR CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 8, no. 4, April 2001 (2001-04), pages 357-368, XP001183179 ISSN: 1097-2765 abstract | 1-39 | | | | |
| A | TRAPANI J A: "Granzymes: a family of lymphocyte granule serine proteases." GENOME BIOLOGY 2001, vol. 2, no. 12, 2001, page REVIEWS3014, XP002305250 ISSN: 1465-6914 abstract | 1-39 | | | | |

information on patent family members

International Application No PCT/DK2004/000282

| | atent document d in search report | | Publication date | | Patent family member(s) | | Publication date |
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| WO | 03010204 | A | 06-02-2003 | EP WO KR | 1417237 03010204 2003010536 | A1 | 12-05-2004 06-02-2003 05-02-2003 |
| US | 6010883 | Α | 04-01-2000 | AT AU CA DE DK EP GB JP JP | 585857 4247485 1340381 3586750 3586750 217985 0161937 | A C D1 T2 A A2 A,B C | 15-10-1992 29-06-1989 21-11-1985 09-02-1999 19-11-1992 22-04-1993 17-11-1985 21-11-1985 18-12-1985 27-09-1995 25-01-1995 23-06-1986 |